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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte RAMKUMAR SUBRAMANIAN,
LINDA HEARNEY PORS,
FEIYAN REN, JASMINE HAN,
and BRIAN L. BARCLAY

Appeal 2009-013063
Application 10/777,415
Technology Center 1600

Decided: February 16, 2010

Before DONALD E. ADAMS, JEFFREY N. FREDMAN, and STEPHEN WALSH, *Administrative Patent Judges*.

FREDMAN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to dosage forms. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

Statement of the Case

Background

"While a variety of sustained release dosage forms for delivering certain drugs exhibiting short half-life may be known, not every drug may be suitably delivered from those dosage forms because of solubility, metabolic processes, absorption and other physical, chemical and physiological parameters that may be unique to the drug" (Spec. 1 ¶ 0003). The Specification teaches that "there are many other approaches to achieving sustained release of drugs from oral dosage forms known in the art" (Spec. 3 ¶ 00010). According to the Specification, these "different approaches include, for example, diffusion systems such as reservoir devices and matrix devices, dissolution systems such as encapsulated dissolution systems . . . and matrix dissolution systems, combination diffusion/dissolution systems and ion-exchange resin systems" (Spec. 3 ¶ 00010).

The Claims

Claims 1-4, 28, and 29 are on appeal. Claim 1 is representative and reads as follows:

> 1. A dosage form comprising
> (a) a membrane defining a compartment, the membrane having an exit orifice formed or formable therein and at least a portion of the membrane being semipermeable;
> (b) an expandable layer located within the compartment remote from the exit orifice and in fluid communication with the semipermeable portion of the membrane;
> (c) a delay layer located adjacent the exit orifice;
> (d) a drug layer located within the compartment between the delay layer and the expandable layer; and

(e) an interface boundary between the delay layer and the drug layer, the interface boundary being convex in shape relative to the exit orifice.

The prior art

The Examiner relies on the following prior art references to show unpatentability:

Theeuwes	US 4,111,202	Sep. 5, 1978
Eckenhoff et al.	US 4,717,566	Jan. 5, 1988
Jao et al.	US 5,252,338	Oct. 12, 1993
Ayer et al.	WO 99/62496 A1	Dec. 9, 1999

FLEXERIL® (CYCLOBENZAPRINE HCL), PHYSICIAN'S DESK REFERENCE 56th Edition 572-573 (2002).

The issues

A. The Examiner rejected claims 1-4 under 35 U.S.C. § 103(a) as obvious over Ayer, Jao, Eckenhoff, and Theeuwes (Ans. 4-7).

B. The Examiner rejected claims 28 and 29 under 35 U.S.C. § 103(a) as obvious over Ayer, Jao, Eckenhoff, Theeuwes and Physician's Desk Reference (Ans. 7).

A. 35 U.S.C. § 103(a) over Ayer, Jao, Eckenhoff, and Theeuwes

The Examiner finds that Ayer discloses "bilayer and trilayer oral osmotic dosage forms. The bilayer has first component layer comprising a selected drug and excipients for forming a deliverable drug composition when hydrated and a second push layer" (Ans. 4). The Examiner finds that Jao teaches "how the polymeric delay layer along with the drug in it helps in delaying the delivery of the drug" (Ans. 5). The Examiner finds that

"Theeuwes teaches an osmotic system for the delivery of active agent over time" (Ans. 6).

The Examiner finds that "Jao et al. do not teach the convex geometry . . . however, Eckenhoff et al. teach a dosage form for delivering a beneficial agent with a convex geometry" (Ans. 5). The Examiner concludes that it would have been obvious to the ordinary artisan to "incorporate a delay layer in place of first drug component in the dosage form of ('496) based on the teachings of Jao" and to "have an interface boundary between the delay layer and the drug layer having a convex configuration as taught by Eckenhoff and Theeuwes because the delay layer helps in delaying the delivery of the active agents" (Ans. 6).

Appellants argue that "none of the cited art shows a dosage form wherein the interface boundary between the delay layer and the drug layer is convex in shape relative to the exit orifice in the dosage form" (App. Br[1]. 4-5). Appellants argue that "a reading of Eckenhoff *et al.* reveals that neither of the convex shaped layers is a delay layer" (App. Br. 5). Appellants argue that the membrane 18 of Theeuwes "is not equivalent to an interface boundary between a delay layer and a drug layer, nor would it serve the equivalent function in a dosage form" (App. Br. 5).

In view of these conflicting positions, we frame the obviousness issue before us as follows:

Have Appellants demonstrated that the Examiner erred in finding it obvious to modify the dosage form of Ayers with "an interface boundary

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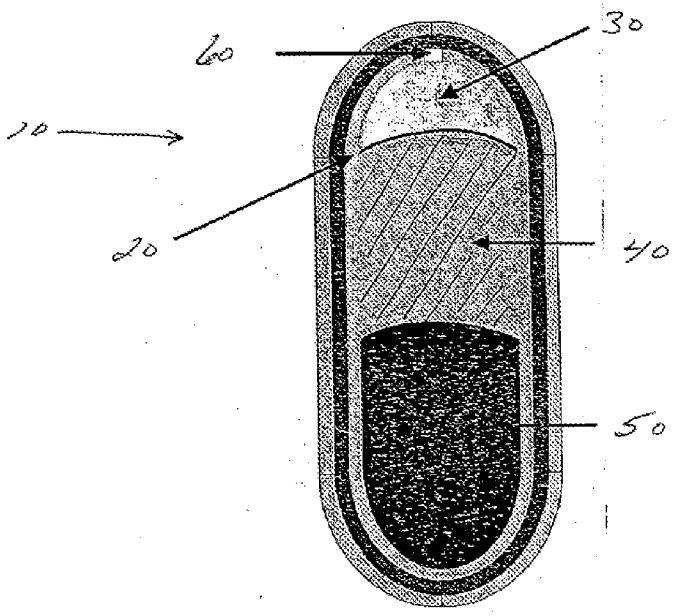
[1] Our page numbering refers to the Appeal Brief as if it was numbered consecutively starting with the first page.

between the delay layer and the drug layer, the interface boundary being convex in shape relative to the exit orifice" as required by Claim 1?

Findings of Fact (FF)

1. The Specification teaches that "the invention comprises layer interface geometry such that each layer interface is convex relative to the orifice. This result is obtained by inverting the traditional compression sequence during manufacturing" (Spec. 11 ¶ 00038).

2. Figure 13 of the Specification discloses the interface geometry as reproduced below:



Inverted Layer Geometry

FIG. 13

"Figure 13 illustrates the preferred layer interface geometry . . . convex relative to the exit orifice" (Spec. 14 ¶ 00058).

3. The Specification teaches that "[d]elay layer 30 comprises osmotically active components, but does not contain drug" (Spec. 20 ¶ 00091).

4. The Specification teaches that "[d]rug layer 40 typically will be a substantially dry . . . composition formed by compression of the carrier, the drug, and other excipients as one layer" (Spec. 22 ¶ 00095).

5. The Specification teaches that "[w]all 20 is formed to be permeable to the passage of an external fluid, such as water and biological fluids, and is substantially impermeable to the passage of cyclobenzaprine, osmagent, osmopolymer and the like" (Spec. 24 ¶ 000105).

6. The Specification teaches that "[p]ush layer 50 . . . comprises an expandable composition in contacting layered arrangement with the second component drug layer 40" (Spec. 28 ¶ 000111).

7. The Specification teaches that the inner wall "is permeable to the passage of gastric fluid entering the compartment defined by wall 20 and provides a lubricating function that facilitates the movement of delay layer 30, drug layer 40 and push layer 50 toward exit 60" (Spec. 30 ¶ 000117).

8. The Specification teaches that the

> traditional compression sequence is inverted, reversed, such that the natural shape of the layer interfaces from compression is inverted to be convex relative to the exit orifice . . . As a result, the localized flow, and subsequent mixing, condition set up by layer hydration at the core-membrane interface is not as significant in impacting the characteristic release profile since the boundary layer-orifice distance is greater. Typically, this reduced effect manifests itself in a more continuous and uniform ascending release profile

(Spec. 34 ¶ 000125).

9. Ayer teaches a "tri-layer tablet core surrounded by a semipermeable membrane and having suitable exit means for releasing drug formulation through the semipermeable membrane" (Ayer 7, ll. 27-29).

10. Ayer teaches that the "tri-layer tablet core has a first drug-containing layer, a second drug-containing layer and a third push layer" (Ayer 7, ll. 29-30). Ayer teaches that the "second component layer is referred to as a 'push' layer since, as fluid is imbibed, the osmopolymer(s) swell and push against the deliverable drug formulation of the first component layer" (Ayer 5, ll. 21-24).

11. Figure 2 of Ayer is reproduced below:

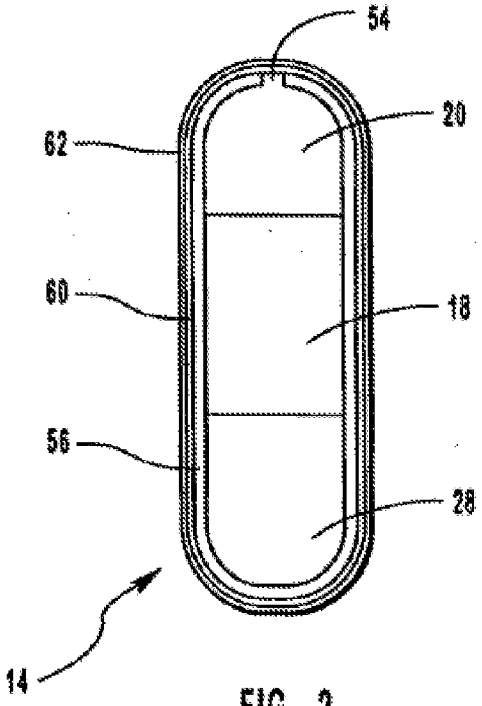


FIG. 2

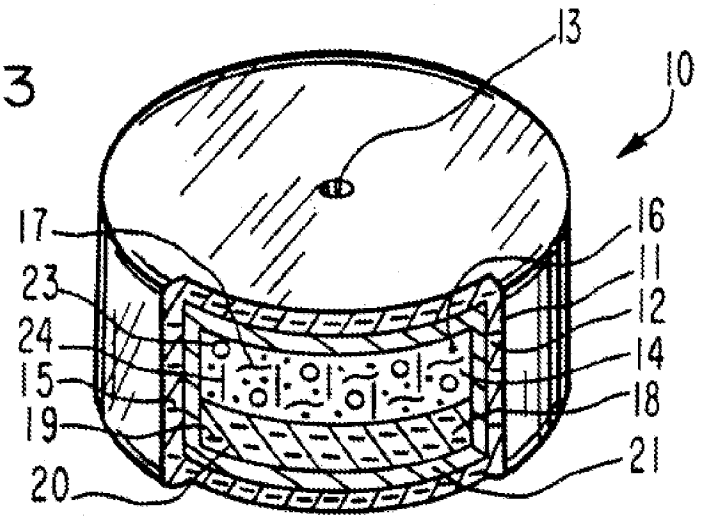
"Figure 2 is a cross-section view of a tri-layer osmotic dosage form" (Ayer 10, l. 5).

12. Ayer teaches that the tri-layer dosage contains "a first component layer 20, containing a selected drug . . . a second component layer 18, containing a higher concentration of drug . . . and a third push layer 28, containing at least one osmopolymer" (Ayer 21, ll. 17-21).

13. Ayer teaches that a "semipermeable membrane 56 surrounds the tri-layer tablet core to form a compartment and a suitably sized orifice 54 is formed through the semipermeable membrane . . . to permit drug formulation to be released from within the compartment" (Ayer 21, ll. 22-25).

14. Figure 3 of Jao is reproduced below:

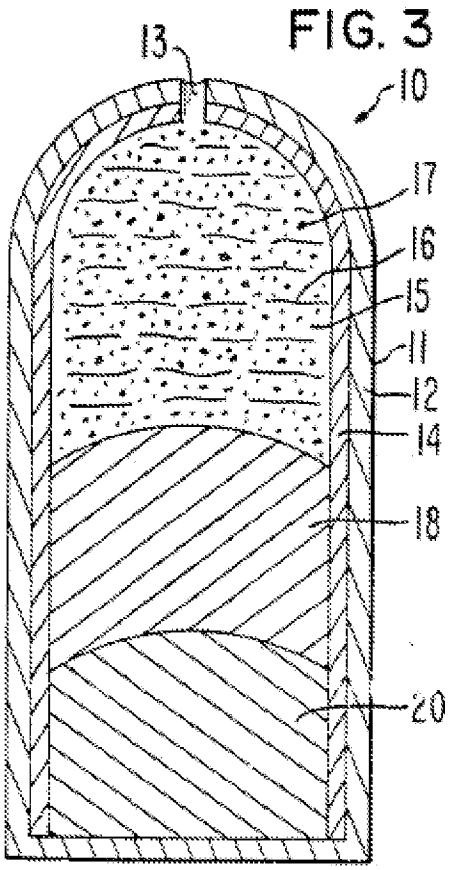
FIG. 3



"FIG. 3 is an opened view of the dosage form . . . for depicting the internal structure of the dosage form, wherein the dosage form comprises an internal coat for delaying drug delivery, which coat surrounds a drug reservoir for delaying the delivery of drug from the reservoir of the dosage form" (Jao 3, ll. 29-34).

15. Jao teaches a "dosage form 10 comprising body 11, wall 12 comprising chemical means 15 for slowing the rate of fluid inhibition through wall 12 into compartment 14, drug 16 in compartment 14, polymeric viscosity governing means 17 in compartment 14, and a second composition 18" (Jao, col. 4, ll. 58-63). Jao teaches that "a delayed drug-delivery dosage form would have a practical application, and it would also represent a valuable contribution to the medical arts" (Jao, col. 2, ll. 12-15).

16. Figure 3 of Eckenhoff is reproduced below:

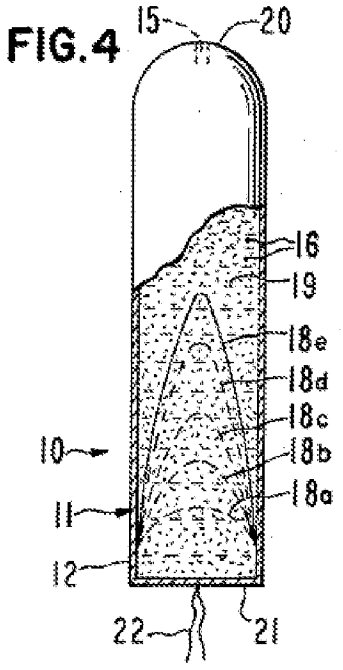


"FIG. 3 is an opened view of the dispensing system 10" (Eckenhoff, col. 5, ll. 34-35).

17. Eckenhoff teaches that "[l]umen 15 further contains an expandable driving member 18 that is in layered contact with a contacting surface 19 of thermo-responsive composition 16" (Eckenhoff, col. 5, ll. 2-4).

18. Theeuwes teaches that "FIG. 4 shows an osmotic system 10 . . . System 10 is structurally identical with system 10 as described above and it has a film 18 that operates in a like manner by being capable of expanding from 18a through 18e" (Theeuwes, col. 6, l. 64 to col. 7, l. 4). The resting position of 18a as illustrated in Figure 4 (reproduced below) is convex.

19. Figure 4 of Theeuwes is reproduced below:



"FIG. 4 shows an osmotic therapeutic system designed for releasing drug" (Theeuwes, col. 4, ll. 13-14).

20. Theeuwes teaches that film 18 "is formed of an expandable material that can move from an initial or rested position . . . through a series

of sequential changes . . . to form fully expanded film 18" (Theeuwes, col. 5, ll. 31-35).

21. Theeuwes further teaches that "compartment 14 by imbibing external fluid 19 across wall 12 continuously increases its volume, thereby exerting a force on film 18 urging it to expand into and diminish the volume of compartment 13, thusly insuring continuous saturation of agent 16 in compartment 13" (Theeuwes, col. 5, ll. 53-57).

Principles of Law

The question of obviousness is resolved on the basis of underlying factual determinations including: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and the prior art; and (4) secondary considerations of nonobviousness, if any. *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966). The Supreme Court has emphasized that "the [obviousness] analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *KSR Int'l v. Teleflex Inc.*, 550 U.S. 398, 418 (2007).

"[W]hen the question is whether a patent claiming the combination of elements of prior art is obvious", *KSR* directs that "a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions." *Id.* at 417.

Analysis

The claims have not been argued separately and therefore stand or fall together. 37 C.F.R. § 41.37(c)(1)(vii). Claim 1 is representative and is

drawn to a dosage form. The claimed dosage form comprises the following five components:

(a) a membrane defining a compartment, the membrane having an exit orifice formed or formable therein and at least a portion of the membrane being semipermeable;

(b) an expandable layer (or push layer (FF 6)) located within the compartment remote from the exit orifice and in fluid communication with the semipermeable portion of the membrane;

(c) a delay layer located adjacent the exit orifice;

(d) a drug layer located within the compartment between the delay layer and the expandable layer; and

(e) an interface boundary between the delay layer and the drug layer, the interface boundary being convex in shape relative to the exit orifice.

Ayer teaches a three layer tablet with a membrane defining a compartment and an exit orifice, a layer adjacent to the exit orifice, a drug layer and a push layer, with the drug layer between the first layer and the push layer (FF 9-13). Jao teaches a first layer which functions as a delay layer in releasing drug (FF 14-15). Accordingly, we find no error in the Examiner's conclusion that it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify Ayer's device to include Jao's "delay layer in place of the first drug component" of Ayer's device (Ans. 6). The ordinary artisan would have reasonably modified Ayer to incorporate a delay layer since Jao teaches that "a delayed drug-delivery dosage form would have a practical application,

and it would also represent a valuable contribution to the medical arts" (Jao, col. 2, ll. 12-15; FF 15).

The Examiner acknowledges that Ayer and Jao "do not teach the convex geometry as claimed" (Ans. 5). However, Eckenhoff and Theeuwes both teach push layers with a convex geometry in order to deliver the drug formulation (FF 16-19). Appellants concede to this point (*see* App. Br. 5 ("Eckenhoff *et al.* and Theeuwes . . . illustrate a convex interface between layers in a dosage form, but not between a drug layer and a delay layer"). We agree with the Examiner that at the time the invention was made it would have been prima facie obvious to a person of ordinary skill in the art to have place a convex interface between every layer of a device as illustrated in Eckenhoff and Theeuwes (FF 16-20). Such a combination is merely a "predictable use of prior art elements according to their established functions." *KSR*, 550 U.S. at 417. For the foregoing reasons, we are not persuaded by Appellants' argument that "none of the cited art shows a dosage form wherein the interface boundary between the delay layer and the drug layer is convex in shape relative to the exit orifice in the dosage form" (App. Br. 4-5).

Appellants also argue that the membrane 18 of Theeuwes "is not equivalent to an interface boundary between a delay layer and a drug layer, nor would it serve the equivalent function in a dosage form" (App. Br. 5). We are not persuaded since Jao teaches an interface boundary between a delay layer and a drug layer (FF 14-15) and since both Eckenhoff and Theeuwes teach that when push layers expand to release drugs, these layers can predictably expand in a convex shape to function to release the desired

drugs (FF 16-21). Further, the membrane of Theeuwes, while located between different layers, functions in "assisting in regulating delivery and the amount of agent 16 from compartment 13" (Theeuwes, col. 5, ll. 27-33; FF 18-21). The membrane therefore functions in the exact same manner as the delay layer of Jao and the drug layer of Ayer and Jao, and is therefore equivalent in function to these layers. *See In re Fout*, 675 F.2d 297, 301 (CCPA 1982) ("Express suggestion to substitute one equivalent for another need not be present to render such substitution obvious.")

Appellants argue that "it is noted that the claimed dosage form provides a more continuous and uniform ascending release profile than observed with dosage forms lacking the convex interface between the delay layer and the drug layer" (App. Br. 6). We are not persuaded. The Specification does not state that this is an unexpected result (FF 8). Our review of Figures 15 and 16 does not show that the release rates show any particularly significant difference in their continuity or uniformity. The showing of unexpected results must be factual; argument or conclusory statements do not suffice. *In re Geisler*, 116 F.3d 1465, 1470 (Fed. Cir. 1997). Unexpected results must also be "commensurate in scope with the degree of protection sought by the claimed subject matter." *In re Harris*, 409 F.3d 1339, 1344 (Fed. Cir. 2005).

In the instant case, Appellants have made no showing that the differences in the geometry of the dosage forms result in any unexpected results. Theeuwes teaches that a convex shape improves and assists in regulating delivery and the amount of agent 16 from compartment (FF 18-21). We do not see the difference between Theeuwes' teaching of elements

18a-e continuously expanding to provide continuous saturation and the continuous and uniform flow as Appellants contend (*see* FF 21). Appellants have not explained why this would be unexpected given the disclosure of Theeuwes. In fact, the portion of the Specification relied upon by Appellants indicates that "[t]ypically" the effects results in increased continuity and uniformity, but does not suggest that this is a necessary result (*see* Spec. 34 ¶ 00125).

Conclusion of Law

Appellants have not demonstrated that the Examiner erred in finding it obvious to modify the dosage form of Ayers with "an interface boundary between the delay layer and the drug layer, the interface boundary being convex in shape relative to the exit orifice" as required by Claim 1.

B. 35 U.S.C. § 103(a) over Ayer, Jao, Eckenhoff, Theeuwes and Physician's Desk Reference

The Examiner relies upon Physician's Desk Reference to teach the use of cyclobenzaprine in the dosage form (*see* Ans. 7). We will affirm this rejection since Appellants do not separately argue these claims and rely upon overcoming the primary rejection over Ayer, Jao, Eckenhoff, and Theeuwes.

SUMMARY

In summary, we affirm the rejection of claim 1 under 35 U.S.C. § 103(a) as obvious over Ayer, Jao, Eckenhoff, and Theeuwes. Pursuant to 37 C.F.R. § 41.37(c)(1)(vii)(2006), we also affirm the rejection of claims 2-4 as these claims were not argued separately. We also affirm the rejection of

claims 28 and 29 under 35 U.S.C. § 103(a) as obvious over Ayer, Jao, Eckenhoff, Theeuwes, and Physician's Desk Reference.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv)(2006).

AFFIRMED

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